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ORIGINAL ARTICLE – BREAST ONCOLOGY

Characteristics and Outcomes of Sentinel Node–Positive Breast Cancer Patients after Total Mastectomy without Axillary-Specific Treatment

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ABSTRACT

Purpose. Regional failure rates are low in patients with a positive sentinel lymph node biopsy (SLNB) who undergo breast-conserving therapy without axillary lymph node dissection (ALND). The applicability of these findings to total mastectomy (TM) patients is not established. Our aims were to evaluate the characteristics and outcomes of SLNB-positive TM patients who did not receive axillary-specific treatment and to compare them to similar patients who underwent breast-conserving surgery (BCS).

Methods. A total of 535 patients with early-stage breast cancer who underwent definitive breast surgery (210 TM, 325 BCS), had a positive SLNB and did not receive ALND between 1997 and 2009 were identified from an institutional database. Characteristics and outcomes were compared between the TM and BCS groups.

Results. Most patients had stage I to IIA, estrogen receptor–positive, progesterone receptor–positive, Her2-negative invasive ductal carcinoma, with minimal nodal disease. Compared to the BCS group, TM patients were younger, had larger tumors, had higher nomogram scores predicting additional axillary disease and were more likely to receive chemotherapy. Ninety-four percent of the BCS cohort and 5 % of the TM cohort received adjuvant radiotherapy. At a median follow-up of 57.8 months, the 4-year local, regional and distant failure rates were 1.7, 1.2 and 0.7 % in the TM group and 1.4, 1.0 and 3.7 % in the BCS group. The 4-year disease-free and overall survival rates were 94.8 and 97.8 % in the TM group and 90.1 and 92.6 % in the BCS group.

Conclusions. Early-stage breast cancer patients with minimal sentinel node disease experience excellent outcomes without ALND, whether they undergo BCS or TM.

Axillary lymph node dissection (ALND) has long been considered the standard of care for clinically node-negative, early-stage breast cancer patients with a positive sentinel lymph node biopsy (SLNB). One rationale for this practice has been to reduce the risk of regional nodal recurrence. However, this logic has been challenged by several recent studies that have reported low rates of axillary failure after omission of ALND in select patients with a positive SLNB.[1–3] Most patients in these trials underwent surgery with thorough margin evaluation and received contemporary systemic and adjuvant radiotherapy (RT). Each of these factors may have contributed to their excellent outcomes.

The best known of these studies is American College of Surgeons Oncology Group (ACOSOG) Z0011, which randomized women with up to 2 positive nodes after breast-conserving surgery (BCS) and SLNB to either ALND or observation. All patients received whole breast RT with standard opposing tangents. Additional supraclavicular or axillary fields were not permitted. With a median follow-up of 6.3 years, regional nodal recurrence rates were equivalent between the arms and less than 1 %.[4]

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Tangential RT was delivered in the supine position, leading to the theory that inclusion of the level I and low level II axillary nodes may have contributed to the excellent axillary control.

The results of ACOSOG Z0011 have stimulated interest in the omission of axillary-specific treatment in other groups, such as total mastectomy (TM) patients. Recently, our center has treated an increasing number of early-stage breast cancer patients with TM and SLNB. Adjuvant RT is not commonly indicated in this setting, making this cohort ideal for analyzing the risk of recurrence in SLNB-positive patients who do not receive any axillary-specific treatment. It must be noted, however, that many of these patients have low-volume nodal disease and therefore are not directly comparable to the ACOSOG Z0011 population. We undertook this study to analyze the characteristics and regional nodal recurrence rates of patients with low-volume sentinel lymph node (SLN) disease who underwent TM without ALND and to compare them to a parallel group treated with BCS ± RT.

MATERIAL AND METHODS

This study design was approved by our institutional review board.

From an institutional database, 3,483 consecutive women were retrospectively identified who had invasive breast cancer, underwent definitive breast surgery at our center between 11/1997 and 5/2009 and had a positive SLNB. A SLNB was defined as positive if carcinoma cells were identified by frozen section, hematoxylin and eosin staining, or immunohistochemistry (IHC). From this group, we excluded 2,795 patients who underwent completion ALND, defined according to surgical intent and/or removal of 10 or more lymph nodes. We also excluded patients who received neoadjuvant chemotherapy, lacked adjuvant therapy details, had N2 disease, had another cancer diagnosis or experienced breast cancer progression before a scheduled ALND. Ultimately, 535 patients comprised our study cohort, of whom 210 underwent TM and 325 underwent BCS.

Lymphatic mapping, lymphoscintigraphy and SLNB were performed as previously described.[5,6] Tumor histology, lymphovascular invasion, estrogen receptor status, progesterone receptor status, HER-2/*neu* status, nuclear grade, margin status, and multifocality or multicentricity were recorded. The probability of additional non-sentinel lymph node metastases was calculated by using a validated nomogram for 526 patients (98.3 %) who had complete pathologic information and fit the nomogram inclusion criteria.[7]

Follow-up consisted of biannual histories and physical examinations. Failures were biopsy-proven. They were defined as local if they occurred in the ipsilateral chest wall or breast and as regional if they occurred in the ipsilateral supraclavicular, axillary or internal mammary lymph nodes.

Fisher's exact and Wilcoxon tests were used to compare characteristics of the TM and BCS patients. Time to local, regional, or distant recurrence and disease-free and overall survival were measured from the date of diagnosis. Patients with no event were censored at the time of their last follow-up. Competing-risks methods were used to calculate local, regional and distant recurrence rates, with death as a competing event, and rates were compared by Gray's test. Kaplan–Meier methods were used to estimate disease-free and overall survival, and differences were tested by the log-rank test. Changes in surgical practice patterns over time were examined by linear regression and the Cochran–Armitage test. All statistical analysis was performed with SAS 9.2 (SAS Institute, Cary, NC) and R 2.11.1 (R Foundation for Statistical Computing, Vienna, Austria) statistical software. P values of <0.05 were considered significant.

RESULTS

As shown in Fig. 1, over the study period, the total number of SLNB-positive patients who did not receive ALND increased with time ($P < 0.0001$). Among this group, the proportion of patients who underwent TM as their definitive surgery increased from 21 % in 1998 to 48 % in 2008 ($P = 0.003$).

Patient and Tumor Characteristics

Patient and disease characteristics of the TM and BCS groups are summarized in Table 1. TM patients were younger, less likely to be white, and more likely to have been evaluated by preoperative magnetic resonance imaging, compared with their BCS counterparts ($P \leq 0.001$).

TM patients had slightly larger tumors than BCS patients (median 1.5 vs. 1.2 cm). Multicentric tumors were more common in TM patients. Close or positive margins were more frequently observed among BCS patients (18 % vs. 8 % close or positive, $P < 0.001$). In the majority of such cases, margin involvement was attributable to tumor at the pectoralis fascia or skin.

In both groups, a median of 3 lymph nodes was dissected and 1 lymph node contained tumor. Sentinel lymph node involvement was predominantly N0(i+) or N1mic, with no difference between the groups (91 % TM vs. 93 % BCS, $P = 0.602$). There was no difference between the two groups in method of detection of nodal metastases (14 % vs. 18 % hematoxylin and eosin staining, 42 % vs. 43 % serial sectioning, 42 % vs. 38 % IHC for TM and

BCS, respectively, $P = 0.405$). TM patients had higher nomogram scores predictive of additional axillary disease (median probability 9 % TM vs. 8 % BCS, $P = 0.003$).

Adjuvant Therapy Characteristics

Sixty-one percent of the entire cohort received chemotherapy, the majority of which was anthracycline and taxane-based (63 %), followed by cyclophosphamide, methotrexate, and 5-fluorouracil (31 %). Compared with BCS patients, a significantly greater proportion of TM patients received chemotherapy (68 % TM vs. 56 % BCS, $P = 0.005$). Seventy-seven percent of all patients received hormone therapy, with no difference between the groups.

There was a significant difference in rates of RT receipt for the TM and BCS groups. Five percent ($n = 10$) of the TM patients and 94 % ($n = 304$) of the BCS patients received adjuvant RT. All 10 of the TM patients were treated to the chest wall and supraclavicular fossa; additionally, two patients received a chest wall boost and one patient received a posterior axillary boost. The median dose was 5000 cGy (range 5000–6040 cGy) in 25 fractions (range 25–30). Among the BCS patients, the techniques used for breast RT were supine standard tangents (54 %), supine high tangents (13 %), prone tangents (22 %), tangents plus a supraclavicular field (0.3 %), tangents plus a supraclavicular field and a posterior axillary boost (2 %), and partial breast irradiation (9 %). The median dose was 5000 cGy (range 4240–6080 cGy) in 25 fractions (range 16–33).

Characteristics of TM patients grouped by receipt of postmastectomy RT (PMRT) are summarized in Table 2. Non-white ethnicity, higher T-stage, close or positive margins and the presence of lymphovascular invasion were significantly associated with receipt of PMRT ($P < 0.05$). TM patients treated with PMRT were more likely to receive chemotherapy than those who did not receive PMRT (100 % vs. 67 %, $P = 0.032$).

Outcomes

Figure 2 illustrates the disease control rates and survival outcomes for the two groups. At a median follow-up of 57.8 months, there were a total of 9 local failures, 6 regional failures, 17 distant failures, and 49 deaths. The median follow-up of the TM group was shorter than that of the BCS group (median 51.3 vs. 61.4 months). There was no significant difference in the cumulative incidence of local and regional failures between the groups ($P = 0.85$ and 0.51), with 4-year local and regional failure rates of 1.7 % vs. 1.4 % and 1.2 % vs. 1.0 % in the TM and BCS groups, respectively. However, the hazard for distant failure was higher in the BCS group ($P = 0.036$), with a 4-year distant recurrence rate of 3.7 % for BCS vs. 0.7 % for TM. Disease-free and overall survival were lower in the BCS group ($P = 0.02$ and 0.002), with 4-year disease-free survival of 94.8 % for TM vs. 90.1 % for BCS and 4-year overall survival of 97.8 % for TM vs. 92.6 % for BCS. Among the 10 TM patients who received PMRT, there were no local, regional, or distant recurrences and no deaths, at a median follow-up of 36 months (range 23–77 months).

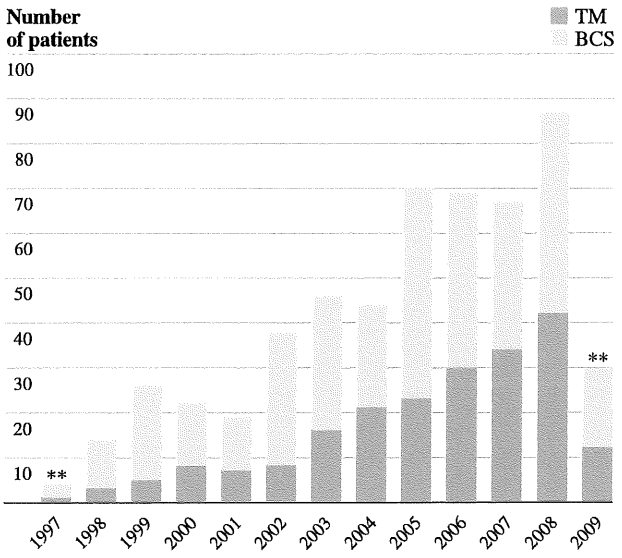

FIG. 1 Number of sentinel lymph node biopsy-positive patients with omission of axillary lymph node dissection by year. The total number of patients increased with time ($P < 0.0001$). The proportion of patients receiving TM as their definitive surgery increased with time ($P = 0.003$). *BCS* breast-conserving therapy, *TM* total mastectomy. **1997 and 2009 were truncated

Outcomes were re-analyzed after excluding the 301 patients with N0(i+) disease, leaving 234 patients (97 TM, 137 BCS) with N1mic or N1 disease for subset analysis. As shown in Fig. 3, the above trends persisted, with no difference in the cumulative incidence of local or regional failure between the TM and BCS groups ($P = 0.42$ and 0.34). The 4-year local failure rates were 1.2 % for TM vs. 1.8 % for BCS, and 4-year regional failure rates were 2.5 % for TM vs. 1.5 % for BCS. Again, the hazard for distant failure was higher in the BCS group, with a 4-year distant-recurrence rate of 4.9 % for BCS vs. 1.5 % for TM; however, this difference no longer reached statistical significance ($P = 0.30$). Disease-free and overall survival were lower in the BCS group ($P = 0.352$ and 0.052), with 4-year disease-free survival of 91.2 % for TM vs. 87.0 % for BCS and 4-year overall survival of 95.1 % for TM vs. 89.7 % for BCS.

The characteristics of the 6 patients in our study cohort who experienced an axillary recurrence are outlined in Table 3. Five of these patients had N1mic and one had macroscopic N1 disease. The median time to a regional recurrence was 27 months, at a median follow-up of

TABLE 1 Patient and treatment characteristics by surgery type

Characteristic	TM ($n = 210$)	BCS ($n = 325$)	*P*-value
Follow-up (months)	51.3 (1.4–154.4)	61.4 (3.7–163.8)	
Median age at diagnosis (years)	54.5 (23–89)	59.0 (28–90)	0.001
Race			<0.001
White	164 (79 %)	289 (89 %)	
Black	24 (12 %)	27 (8 %)	
Asian	20 (10 %)	6 (2 %)	
Other	2 (1 %)	3 (1 %)	
MRI before definitive surgery			0.001
No	121 (58 %)	233 (72 %)	
Yes	89 (42 %)	92 (28 %)	
No. of BCS attempts			
0	158 (75 %)	0 (0 %)	
1	36 (17 %)	219 (67 %)	
2	14 (7 %)	96 (30 %)	
≥3	2 (1 %)	10 (3 %)	
Tumor size (cm)	1.5 (x*-7.0)	1.2 (x*-4.5)	0.016
No. with tumor size missing	2	4	
T stage			<0.001
Tx	1 (0.5 %)	1 (0.3 %)	
T1	144 (69 %)	276 (85 %)	
T2	63 (30 %)	48 (15 %)	
T3	2 (1 %)	0	
Total no. (range) of SLN dissected	3 (1–9)	3 (1–9)	0.081
Total no. (range) of positive SLN	1 (1–3)	1 (1–3)	0.092
N stage			0.602
N0(i+)	113 (54 %)	188 (58 %)	
N1mic	78 (37 %)	113 (35 %)	
N1	19 (9 %)	24 (7 %)	
Method of detection			0.577
Frozen section	2 (1 %)	1 (0.3 %)	
Routine H&E	30 (14 %)	60 (18 %)	
Serial sectioning	89 (42 %)	139 (43 %)	
IHC only	89 (42 %)	125 (38 %)	
Median (range) MSKCC nomogram score	9 (1–70)	8 (2–85)	0.003
No. with MSKCC nomogram score missing	5	4	
Tumor histology			0.283
IDC	156 (74 %)	262 (80 %)	
ILC	42 (20 %)	46 (14 %)	
Mixed	10 (5 %)	15 (5 %)	
Other	2 (1 %)	2 (1 %)	
Final margin status			<0.001
Negative	194 (92 %)	266 (82 %)	
Close	14 (7 %)	37 (11 %)	
Positive	2 (1 %)	22 (7 %)	
Multicentric/multifocal			<0.001
No	87 (41 %)	279 (86 %)	
Yes ($n = 169$)	123 (59 %)	46 (14 %)	
Multifocal	42 (34 %)	45 (98 %)	
Multicentric	81 (66 %)	1 (2 %)	
Lymphovascular invasion			0.111
Absent	155 (74 %)	260 (80 %)	
Present	55 (26 %)	65 (20 %)	
Nuclear grade			0.099
I	13 (8 %)	16 (6 %)	
II	76 (48 %)	162 (58 %)	
III	70 (44 %)	100 (36 %)	
Missing	51	47	
Estrogen receptor			0.159
Negative	35 (17 %)	39 (12 %)	
Positive	174 (83 %)	281 (88 %)	
Unknown	1	5	
Progesterone receptor			0.327
Negative	66 (32 %)	87 (27 %)	
Positive	143 (68 %)	231 (73 %)	
Unknown	1	7	
Her2-neu			0.058
Negative	174 (86 %)	276 (91 %)	
Positive	29 (14 %)	26 (9 %)	
Unknown	7	23	
Chemotherapy			0.005
No	67 (32 %)	144 (44 %)	
Yes	143 (68 %)	181 (56 %)	
Chemotherapy type ($n = 324$)			0.203
CMF or MF	38 (27 %)	62 (34 %)	
Anthracycline	4 (3 %)	9 (5 %)	
Anthracycline and taxane	97 (69 %)	103 (58 %)	
Other	2 (1 %)	5 (3 %)	
Missing	2	2	
Hormone therapy			0.753
No	50 (24 %)	73 (23 %)	
Yes	159 (76 %)	250 (77 %)	
Missing	1	2	
Radiotherapy			<0.001
No	200 (95 %)	21 (67 %)	
Yes	10 (5 %)	304 (94 %)	

BCS breast-conserving surgery, *CMF* cyclophosphamide, methotrexate, and fluorouracil, *H&E* hematoxylin and eosin, *IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *MF* methotrexate and fluorouracil, *MRI* magnetic resonance imaging, *IHC* immunohistochemistry, *MSKCC* Memorial Sloan-Kettering Cancer Center, *SLN* sentinel lymph node, *TM* total mastectomy

[a] Data are presented as *n* (%) or median (range). * One patient in each group had Tx disease

TABLE 2 Characteristics of TM patients by receipt of PMRT

Characteristic	No PMRT ($n = 200$)	PMRT ($n = 10$)	*P*-value
Follow-up (mo)	54.4 (1.4–154.4)	36.1 (23.2–76.9)	
Median age at diagnosis (y)	55 (23–89)	55 (30–77)	0.442
Race			0.009
White	159 (80 %)	5 (50 %)	
Black	19 (10 %)	5 (50 %)	
Asian	20 (10)	0 (0 %)	
Other	2 (1 %)	0 (0 %)	
T stage			0.005
Tx	0	1 (10 %)	
T1	139 (70 %)	5 (50 %)	
T2	61 (30 %)	2 (20 %)	
T3	2 (1 %)	2 (20 %)	
Total no. of SLN dissected	3 (1–9 %)	4 (1–7 %)	0.183
Total no. of positive SLN	1 (1–3 %)	1 (1–2 %)	0.357
N stage			0.471
N0(i+)	106 (53 %)	7 (70 %)	
N1mc	76 (38 %)	2 (20 %)	
N1	18 (9 %)	1 (10 %)	
Median (range) MSKCC nomogram score	9 (1–70 %)	13 (4–31 %)	0.088
No. with MSKCC nomogram score missing	4	1	
Tumor histology			0.696
IDC	149 (75 %)	7 (70 %)	
ILC	39 (20 %)	3 (30 %)	
Mixed	10 (5 %)	0 (0 %)	
Other	2 (1 %)	0 (0 %)	
Final margin status			0.004
Negative	188 (94 %)	6 (60 %)	
Close	11 (6 %)	3 (30 %)	
Positive	1 (0.5 %)	1 (10 %)	
Multicentric/multifocal			0.528
No	84 (42 %)	3 (30 %)	
Yes ($n = 123$)	116 (58 %)	7 (70 %)	
Multifocal	39 (34 %)	3 (43 %)	
Multicentric	77 (66 %)	4 (57 %)	
Lymphovascular invasion			0.022
Absent	151 (76 %)	4 (40 %)	
Present	49 (24 %)	6 (60 %)	
Nuclear grade			0.842
I	13 (9 %)	0 (0 %)	
II	73 (48 %)	3 (43 %)	
III	66 (43 %)	4 (57 %)	
Missing	48	3	
Estrogen receptor			0.676
Negative	33 (17 %)	2 (20 %)	
Positive	166 (83 %)	8 (80 %)	
Unknown	1	0	
Progesterone receptor			0.728
Negative	662 (31 %)	4 (40 %)	
Positive	137 (69 %)	6 (60 %)	
Unknown	1	0	
Her2-neu			0.363
Negative	164 (85 %)	10 (100 %)	
Positive	29 (15 %)	0 (0 %)	
Unknown	7	0	
Chemotherapy			0.032
No	67 (34 %)	0 (0 %)	
Yes	133 (67 %)	10 (100 %)	
Chemotherapy type ($n = 143$)			0.824
CMF or MF	36 (28 %)	2 (20 %)	
Anthracycline	4 (3 %)	0 (0 %)	
Anthracycline and taxane	89 (68 %)	8 (80 %)	
Other	2 (1 %)	0 (0 %)	
Missing	2	0	
Hormone therapy			1.000
No	48 (24 %)	2 (20 %)	
Yes	151 (76 %)	8 (80 %)	

CMF cyclophosphamide, methotrexate, and fluorouracil, *IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *MF* methotrexate and fluorouracil, *MSKCC* Memorial Sloan-Kettering Cancer Center, *SLN* sentinel lymph node, *TM* total mastectomy, *PMRT* postmastectomy radiotherapy

[a] Data are presented as *n* (%) or median (range)

57.8 months. Of the 3 TM patients who recurred, 2 received doxorubicin and cyclophosphamide followed by paclitaxel (AC-T), whereas 1 declined any systemic therapy. None received PMRT. Of the 3 BCS patients who recurred, 1 received AC-T chemotherapy, and the other 2 received endocrine therapy alone. Two of the 3 patients received whole breast RT with standard opposing tangential beams in the supine position, while the third declined RT because of other comorbidities.

DISCUSSION

Over the past decade, the pattern of management of early-stage breast cancer has been toward less radical surgeries. As one step along this path, axillary management has undergone a recent paradigm shift. The results of ACOSOG Z0011 suggest that ALND can be avoided for clinically

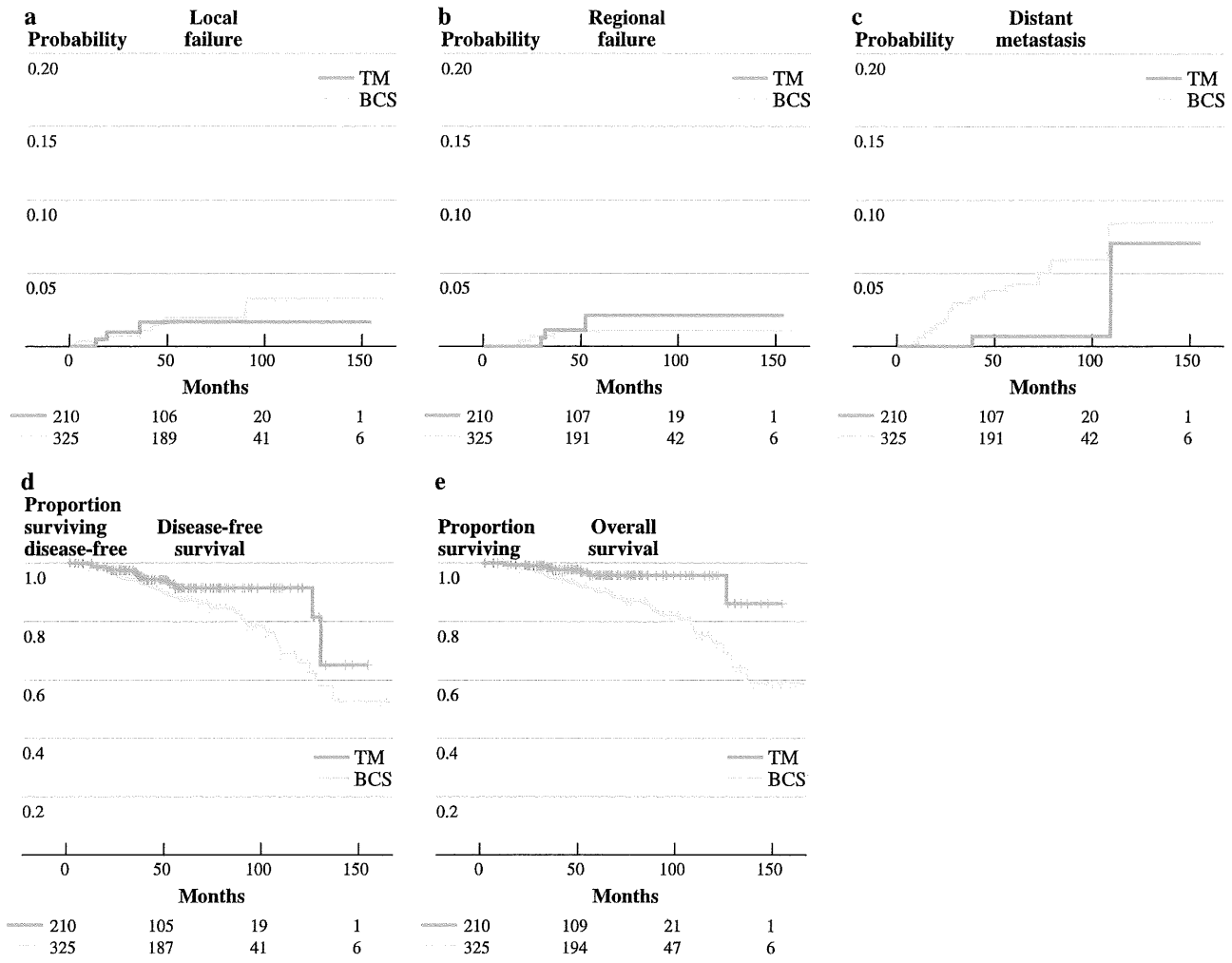

FIG. 2 Cumulative incidence and Kaplan–Meier curves for disease outcomes by surgery type. **a** $P = 0.85$. **b** $P = 0.51$. **c** $P = 0.036$. **d** $P = 0.02$. **e** $P = 0.002$. *BCS* breast-conserving therapy, *TM* total mastectomy

node-negative patients with up to 2 macroscopically positive sentinel nodes, who undergo breast-conserving therapy. All patients in ACOSOG Z0011 were treated with whole breast RT in the supine position, leading to the theory that irradiation of the lower axilla contributed to the low regional failure rates. We have previously shown that regional control was excellent among SLNB-positive breast-conserved patients who did not receive ALND and were treated with whole breast RT in the prone position.[8] This techniques does not deliver any appreciable radiation dose to the axilla; thus, these findings challenge the hypothesis that axillary irradiation is responsible for the low regional recurrence rates.

We now report the outcomes of early-stage breast cancer patients with SLNB-positive disease who underwent TM without ALND. Analysis of this cohort allowed us to bypass any confounding effect of adjuvant RT, because it is infrequently indicated for TM patients with small tumors and low-volume nodal disease. Changing practice patterns have led to the accumulation of such patients at our center. First, several studies suggest that mastectomy rates for early-stage breast cancer patients have increased, the reasons for which are multifactorial but influenced by patient preference.[9,10] In contrast, rates of completion ALND in SLNB-positive patients have declined over the past decade, a trend observed in both BCS and TM patients (Fig. 1).[11]

In our study, TM patients experienced excellent outcomes in the absence of ALND and with rare receipt of adjuvant RT. Furthermore, their local and regional failure rates did not differ significantly from those of analogous BCS patients, the majority of whom did receive adjuvant RT. Four-year local and regional failure rates were 1.7 and 1.2 % among TM patients and 1.4 and 1.0 % among BCS patients. These results expand upon the 0–1.4 % rates of regional nodal recurrence observed in published series of SLNB-positive patients who did not receive ALND, which have included small numbers of TM patients.[1–3]

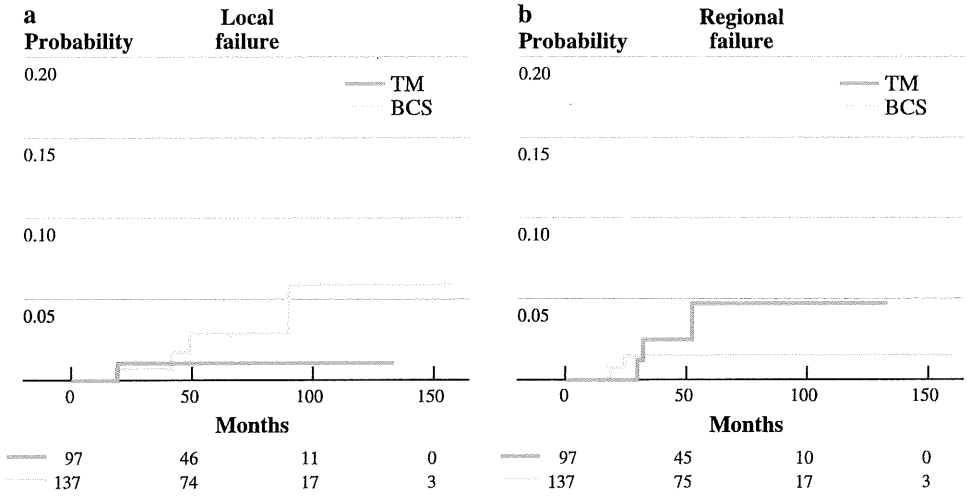

FIG. 3 Cumulative incidence of local and regional recurrence by surgery type for N1mic and N1 patients. **a** $P = 0.42$. **b** $P = 0.34$. *BCS* breast-conserving therapy, *TM* total mastectomy

TABLE 3 Clinical and pathologic characteristics of patients with regional recurrence

Age at diagnosis (years)	Surgery type	Histology	T stage	N stage	ER status	PR status	Her2 status	CT	RT	HT	Mo. to recurrence
43	TM	IDC	T2	N1mic	+	+	−	ACT	None	Yes	31.7
43	TM	IDC	T1mic	N1mic	−	−	−	−	None	No	29.8
78	TM	IDC	T1a	N1mic	−	−	+	ACT	None	No	24.9
49	BCS	IDC	T2	N1mic	+	−	−	−	ST	Yes	35.9
70	BCS	ILC	T1c	N1	+	−	−	−	ST	Yes	18.2
72	BCS	IDC	T1c	N1mic	−	+	+	ACT	None	No	20.0

ACT doxorubicin and cyclophosphamide, followed by paclitaxel/docetaxel, *BCS* breast-conserving surgery, *CT* chemotherapy, *ER* estrogen receptor, *HT* hormone therapy, *IDC* invasive ductal carcinoma, *ILC* invasive lobular carcinoma, *PR* progesterone receptor, *RT* radiotherapy, *ST* standard tangents in the supine position, *TM* total mastectomy

We compared the TM and BCS patients to discern any clinical and pathological differences between the two groups. Not surprisingly, patients who underwent TM had slightly larger tumors, a higher frequency of multicentric or multifocal disease and nominally higher nomogram scores than their BCS counterparts. Interestingly, black patients were more likely to receive TM and undergo PMRT than non-black patients. Disease characteristics between black vs. other ethnicity patients were well balanced, except for a lower incidence of estrogen receptor (ER)-positive tumors (69 % ER-positive in black vs. 87 % in all other races, $P = 0.015$). We speculate that the higher incidence of ER-negative tumors in black patients may have influenced practitioners to recommend more aggressive local therapy in this population. There were no significant differences in the outcomes by race.

Although the TM patients had more adverse pathologic features, they had a lower hazard for distant failure. The greater use of chemotherapy among TM patients likely mitigated these risk factors and led to a reduced risk of systemic recurrence. Additionally, the TM patients were younger and likely had fewer comorbidities, which may have contributed to their better overall survival.

The majority of patients in both groups had minimal nodal disease. Fifty-four percent of TM patients and 58 % of BCS patients had N0(i+) disease. Although studies such as ACOSOG Z010 and national surgical adjuvant breast and bowel project (NSABP) B-32 recently established the low prognostic significance of isolated tumor cells in the sentinel node, their impact on the decision for ALND and administration of adjuvant systemic therapy was an evolving issue over the past decade. Van Deurzen et al. observed a pooled overall risk of non-SLN involvement in 12.3 % of patients with isolated tumor cell-only disease, 63.5 % of which were macrometastases.[12] In a study of patients with occult SLN metastases treated during an

earlier era at our institution, patients with N0(i+) sentinel nodes had significantly worse disease-free survival compared with patients with N0 disease.[13] In light of these data and the uncertainty regarding the benefit of ALND during the earlier years of the study, we chose to include N0(i+) patients in our study population.

When our analysis was limited to patients with N1mic or N1 disease, the 4-year regional recurrence rates were 1.5 % for BCS and 2.5 % for TM at 4 years, with no significant difference between the two groups (Fig. 3). Thus, regional failure rates were only slightly higher after the exclusion of N0(i+) patients.

Several caveats must be considered when interpreting these results. Our study population represents a select group of patients whose risk of additional axillary metastases was low. Although no formal institutional guidelines existed during the study period, there was a tendency to omit ALND in SLNB-positive patients who were elderly and had ER-positive disease, IHC-detected nodal involvement, small tumors, and low Memorial Sloan-Kettering Cancer Center nomogram scores.[14,15] Because these patients were identified as being at low risk of axillary failure, omission of ALND was deemed to be safe. In our study population, the median risk of non-SLN axillary nodal metastases was 8 %. Thus, the majority of patients likely had no residual axillary disease after the SLNB. Furthermore, in contrast to the NSABP B04 study, in which half of patients with residual nodal disease developed a clinical axillary failure in the absence of systemic therapy, the majority of our patients did receive systemic therapy.[16] Therefore, we anticipate an even lower risk of clinically apparent locoregional recurrence among the small proportion of patients in our study population who had residual pathologic nodal disease. Our results should not be extrapolated to populations at a higher risk of regional recurrence. Furthermore, in our study population, TM patients were at a higher risk of harboring additional axillary disease than analogous BCS patients, emphasizing the importance of exercising caution when omitting axillary-specific treatment in this group.

Our study is not the first to suggest that low-risk patients who undergo TM may avoid axillary-specific treatment. The International Breast Cancer Study Group Trial 10–93 compared axillary clearance versus no axillary treatment in a population of clinically node-negative breast cancer patients $\geq$60 years old, nearly half ($n = 211$) of whom underwent TM as their definitive surgery and all of whom received adjuvant tamoxifen. At a median follow-up of 6 years, axillary recurrence rates were 1 % in the arm that received ALND and 3 % in the arm that received no axillary treatment. Disease-free survival and overall survival were similar between the two groups. However, outcomes in the TM patients were not reported separately.[17]

Lastly, the infrequent use of RT among our TM cohort does not mean that there is no role for PMRT in patients with low-volume sentinel node disease. Adverse features such as large tumor size, presence of lymphovascular invasion, and involvement of surgical margins were associated with receipt of PMRT. The low number of regional failure events and the non-random assignment of treatment limit the ability to draw any definitive conclusions about the efficacy of PMRT; nonetheless, it is notable that all three of the TM patients who experienced regional nodal failure had N1mic disease and had not received PMRT and that none of the 10 patients who received PMRT experienced a disease recurrence. This underscores the importance of refining selection criteria for PMRT in patients with minimal nodal disease.

In conclusion, TM patients with low-volume sentinel node disease experienced low regional failure rates, despite the lack of axillary dissection and rare axillary irradiation. The 4-year rate of regional nodal failure in these patients was 1.2 %, similar to that of analogous patients undergoing breast-conserving therapy. Omission of axillary-specific treatment may be possible in this select group of patients. Future studies comparing the outcomes of mastectomy patients with a positive SLNB treated with and without ALND will be helpful in identifying those patients who may benefit from additional therapy and those who may avoid over-treatment.

CONFLICTS OF INTEREST None.

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